Technical Abstract

Abstract: A cell-line was established from the neoplastic cells of a patient with malignant melanoma. The cells were obtained during the natural course of the patient's treatment. The melanoma cells express defined MHC Class I histocompatibility determinants. The gene for human interleukin-2 (IL-2) was transduced into the cells with the aid of a replication-defective retrovirus. Integration of the gene into genomic DNA and its expression were established. The IL-2-secreting cell-line was found to be free of recombinant retro-viruses and infectious agents. It will be X-irradiated (5000 rads) and then used to immunize twelve informed patients with Stage IV malignant melanoma in a Phase I toxicity study.

Patients will become eligible for inclusion in this study only if they develop metastatic melanoma and have failed all standard forms of treatment. The IL-2-secreting melanoma cells will be injected into patients who differ in at least three of six alleles at the Class I locus. The patient's anti melanoma immune response to the injected cells will be determined by both *in vivo* and *in vitro* parameters. Background studies performed in inbred mice indicate that X-irriadated IL-2-secreting cells that express both melanoma-associated antigens and allogeneic Class I histocompatability antigens are more antigenic in terms of their capacity to induce an anti melanoma response than X-irradiated melanoma cells. Of significance for the future potential of this form of therapy, the period of survival of mice with established melanoma was significantly ($P < 0.001$) longer than that of untreated animals or animals treated with X-irradiated melanoma cells. There was no evidence that immunizations with the IL-2-secreting cells were toxic to the tumor-bearing recipients.